Wheeler et al.

Application No.: 09/431,594

Page 2

- 43. (New) The nucleic acid-lipid particle of claim 42, wherein said nucleic acid in said particle is resistant in agreeous solution to degradation with a nuclease.
- 44. (New) The nucleic acid-lipid particle of claim 42, wherein said particle is substantially non-toxic.
- 45. (New) The nucleic acid-lipid particle of claim 42, wherein said particle has a median diameter of less than about 150 nm.
- 46. (New) The nucleic acid-lipid particle of claim 42, wherein said cationic lipid is a member selected from the group consisting of N,N-dioleyl-N,N-dimethylammonium chloride (DODAC), N,N-distearyl-N,N-dimethylammonium bromide (DDAB), N-(1-(2,3-dioleyloxy)propyl)-N,N,N-trimethylammonium chloride (DOTAP), N-(1-(2,3-dioleyloxy)propyl)-N,N,N-trimethylammonium chloride (DOTMA), and N,N-dimethyl-2,3-dioleyloxy)propylamine (DODMA), and a mixture of two or more of the above.
- 47. (New) The nucleic acid-lipid particle of claim 42, wherein said particle further comprises an additional non-cationic lipid.
- 48. (New) The nucleic acid-lipid particle of claim 47, wherein said non-cationic lipid is selected from the group consisting of DOPE, POPC, and EPC.
- 49. (New) The nucleic acid-lipid particle of claim 42, wherein said conjugated lipid is a PEG-lipid.
- 50. (New) The nucleic acid-lipid particle of claim 49, wherein said PEG-lipid comprises from 1% to about 15% of the lipid present in said particle.
- 51. (New) The nucleic acid-lipid particle of claim 49, wherein said PEG-lipid is PEG-ceramide.
- 52. (New) The nucleic acid-lipid particle of claim 51, wherein the ceramide of said PEG-ceramide comprises a fatty acid group having 8 carbon atoms.

ort.

Wheeler et al.

Application No.: 09/431,594

Page 3

- 53. (New) The nucleic acid-lipid particle of claim 51, wherein the ceramide of said PEG-ceramide comprises a fatty acid group having 14 carbon atoms.
- 54. (New) The nucleic acid-lipid particle of claim 51, wherein the ceramide of said PEG-ceramide comprises a fatty acid group having 20 carbon atoms.
- 55. (New) The nucleic acid-lipid particle of claim 49, wherein said PEG-lipid is PEG-phosphatidylethanolamine.
- 56. (New) The nucleic acid-lipid particle of claim 42, wherein the nucleic acid:lipid ratio within said particle is at least 5 mg nucleic acid per mmol lipid.
- 57. (New) The nucleic acid-lipid particle of claim 42, wherein the nucleic acid:lipid ratio within said particle is at least 20 mg nucleic acid per mmol lipid.
- 58. (New) The nucleic acid-lipid particle of claim 42, wherein the nucleic acid:lipid ratio within said particle is at least 40 mg nucleic acid per mmol lipid.
- 59. (New) The nucleic acid-lipid particle of claim 42, wherein said nucleic acid is DNA.
- 60. (New) The nucleic acid-lipid particle of claim 42, wherein said nucleic acid is a plasmid.
- 61. (New) The nucleic acid-lipid particle of claim 42, wherein said nucleic acid is an antisense oligonucleotide.
- 62. (New) The nucleic acid-lipid particle of claim 42, wherein said nucleic acid is a ribozyme.
- 63. (New) The nucleic acid-lipid particle of claim 42, wherein said cationic lipid comprises 50% or less of the lipid present in said particle.
- 64. (New) The nucleic acid-lipid particle of claim 42, wherein said cationic lipid comprises from 0% to about 20% of the lipid present in said particle.

Cont

525

Wheeler et al.

Application No.: 09/431,594

Page 4

- 65. (New) The nucleic acid-lipid particle of claim 42, wherein the nucleic acid component of said particle is substantially not degraded after exposure of said particle to a nuclease at 37° C for 20 minutes.
- 66. (New) The nucleic acid-lipid particle of claim 42, wherein the nucleic acid component of said particle is substantially not degraded after incubation of said particle in serum at 37° C for 30 minutes.
- 67. (New) The nucleic acid-lipid particle of claim 42, wherein more than 10% of a plurality of such particles are present in plasma one hour after intravenous administration.
- 68. (New) The nucleic acid-lipid particle of claim 42, wherein transformation of cells by said particle at a site distal to the site of administration is detectable for at least four days after intravenous injection.
- 69. (New) A pharmaceutical composition comprising a nucleic acid-lipid particle and a pharmaceutically acceptable carrier, said nucleic acid-lipid particle comprising a cationic lipid, a conjugated lipid that inhibits aggregation of particles, and a nucleic acid.
- 70. (New) The pharmaceutical composition of claim 69, wherein said cationic lipid is selected from the group consisting of N,N-dioleyl-N,N-dimethylammonium chloride (DODAC), N,N-distearyl-N,N-dimethylammonium bromide (DDAB), N-(1-(2,3-dioleyloxy)propyl)-N,N,N-trimethylammonium chloride (DOTAP), N-(1-(2,3-dioleyloxy)propyl)-N,N,N-trimethylammonium chloride (DOTMA), and N,N-dimethyl-2,3-dioleyloxy)propylamine (DODMA), and a mixture of two or more of the above.
- 71. (New) The pharmaceutical composition of claim 69, wherein said particle further comprises an additional non-cationic lipid.
- 72. (New) The pharmaceutical composition of claim 71, wherein said additional non-cationic lipid is selected from the group consisting of DOPE, POPC, and EPC.

al Cont.